

## CANCER OF THE LIP\*

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LIKE malignant disease elsewhere, cancer of the lip is a grave disease. It metastasizes to regional lymph nodes and will eventually kill the patient unless it is treated adequately and at an early stage. Fortunately an ulcer or a growth on the lip continually reminds the patient of its presence. It can usually be easily recognized by the physician, although some of the early lesions arising from an area of hyperkeratosis may not be clinically so evident. Because of its accessibility, it lends itself to a number of ways of treatment. For these reasons its radiological management presents an interesting problem.

This paper is a review of some 534 cases of cancer of the lip which have been treated radiologically. It comprises the consecutive cases seen in the Saskatchewan Cancer Clinics of Regina and Saskatoon to the end of 1943. All cases included in this series have had their cancers proved by histological examination of a biopsy specimen. All patients have had their entire treatment carried out at one or other of the above mentioned clinics. There were some cases, particularly in the early years, who were treated on clinical grounds alone. They are not included in this series.

Cancer of the lip is a common form of malignant disease. Of 2,254 consecutive cases of malignant disease seen in the Saskatoon Clinic, 254 of 11.3%, were patients who had a cancer of the lip. Martin<sup>1</sup> of the Memorial Hospital, New York, reports cancer of the lip to comprise 4% of all their cancer admissions, while Ackerman and Regato<sup>2</sup> report cancer of the lip to represent between 25 and 30% of all forms of cancer of the oral cavity.

It affects all age groups. The youngest patient in this series was 22 years of age, while the oldest was 86. The mean age was 57 years. The greatest number of patients fell in the decade between 50 and 59 years of age (Fig. 1; Table I).

However, when we compare the percentage of cases in each age group with the percentage of

the population in each age group (Fig. 2), we find the incidence of cancer of the lip to increase with age.

In our series there is a slight decline over 80 years of age, but this may be statistically insignificant, since there were only 14 patients over 80 years of age.

Cancer of the lip is predominantly found in men. There were 527 male (98.6%) as compared to 7 (or 1.4%) of female patients. Cross *et al.*<sup>3</sup> report 2% female patients from the Pondville Hospital whereas Howes and La Rosa<sup>4</sup>

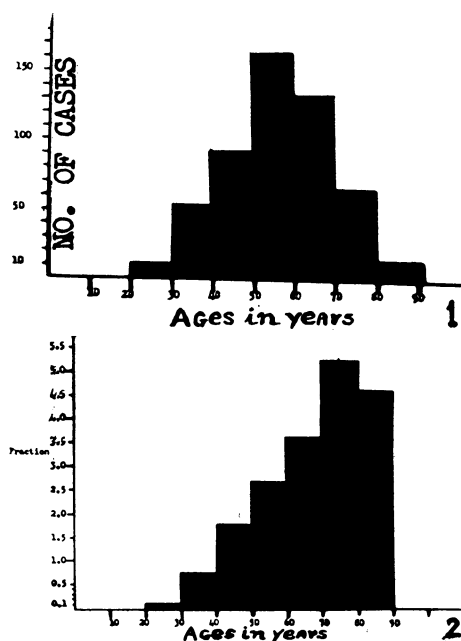


Fig. 2.—Fraction: percentage of patients in each age group to the percentage of the male population in each age group, multiplied by 1,000.

TABLE I.  
AGE DISTRIBUTION

20 - 29 years	10
30 - 39 years	53
40 - 49 years	92
50 - 59 years	165
60 - 69 years	133
70 - 79 years	67
80 - 89 years	14
Total	534

report 1.7%. Of interest in this respect is a report from Radiumhemmet in Stockholm where cancer of the lower lip is common in women—Martin<sup>1</sup> quotes a figure of 16% in this respect.

Most reports mention the predominance of cancer of the lip in outdoor workers who present a long history of outside exposure. There were 476 patients, in the present series, who belonged to this class. Of greater value, however, is the

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fact that 440 of these, or 82% of the total number of cases, were farmers. The Dominion Bureau of Statistics report that only 67.5% of the male population of Saskatchewan, over 14 years of age, were gainfully employed in agriculture in 1941 (a representative year in our survey). That is, there were 2.1 times as many farmers in Saskatchewan as male persons of other occupations. However cancer occurred 4.5 times more frequently among farmers than these others. That is, cancer occurred 2.15 times more frequently among this occupational group than in the rest of the male population.

Only 6 (1.1%) of these patients had a positive Wassermann reaction. This is less than reported in most series (Martin<sup>1</sup> 10% Cross<sup>3</sup> 7.2%).

Most of the cases occurred on the lower lip (97%) as is usually the case. Martin<sup>1</sup> reports 93% while Cross *et al.*<sup>3</sup> report 97% for lower lip and commissural lesions. Martin rather stresses that 56% of his series occurred on the left side of the lower lip, although reports in the older literature indicated a right-sided preponderance. In the present series the distribution was as follows:

TABLE II.  
SITE OF LESION

Right lower lip .....	198
Left lower lip .....	213
Mid lower lip .....	93
Whole lower lip .....	11
Lower lip (not specified) .....	5
Upper lip .....	14
Total .....	534

We do not feel that such a distribution is of any statistical importance in an etiological study.

Many patients had a long history of a pre-existing lip disease; 24.5% or 131 patients, had a definite history of having had a chronic ulcer, leukoplakia, recurring cracks, keratosis, or chronic epithelial hyperplasia before the development of the cancer. The duration of these lesions varied from 9 months to as long as 20 years. The average duration was 46 months. When the above patients are excluded, 343 (64%) of the patients gave the duration of the lesion from one month to one year with the mean duration as 4.8 months and the median duration as 3 months. Fourteen patients with carcinoma of the upper lip had their lesions for an average of 5.7 months before presenting themselves for treatment. Of the 15 patients

who had significantly enlarged nodes when originally seen, the average delay in seeking treatment was 23 months. In 31 cases the duration of the lesion was not specified (Table III).

TABLE III.  
AVERAGE DELAY PRIOR TO TREATMENT

	No. of cases	% of total	Average delay
No history of pre-existing lesions .....	343	64.2	4.8 mons.
History of pre-existing chronic lesion .....	131	24.5	46.0 mons.
Significantly enlarged nodes when originally seen .....	15	2.8	23.0 mons.
Carcinoma of upper lip .....	14	2.6	5.7 mons.
Duration not specified .....	31	5.8	.....
Total .....	534	100.0	

*Pathology.*—Carcinoma of the lip is almost invariably an epidermoid carcinoma. In the present series this was the histological diagnosis in 529 cases. One patient was reported to have an intra-epidermal carcinoma (Bowen's disease), one a carcinoma *in situ*, one a basosquamous carcinoma and two were reported as basal cell carcinomata. These latter two are worthy of further mention.

#### CASE 1

A 45-year old female patient presented herself with a history of having a sore on the right side of the lower lip for the past 5 years. She was definite that it first started on the vermillion surface from where it spread to involve the skin just below. On examination, a lesion with the appearance of a basal cell carcinoma was present at the mucocutaneous junction. There was some scarring on the vermillion surface of the lip adjacent to it. Clinical diagnosis: "Cicatrizing rodent ulcer". Pathological report: basal cell carcinoma.

#### CASE 2

A 48-year old male patient who had had a small growth on the mucosal surface of the upper lip for 4 years. Recently it had become superficially ulcerated. On examination, the patient had a 1 cm. lesion on the mucosal aspect of the upper lip. The lip had to be everted in order to expose the lesion. Clinical diagnosis: "Ulcerated mucous cyst". Pathological diagnosis: basal cell carcinoma.

Martin<sup>1</sup> states that basal cell carcinomas never arise in mucous membrane. Whether the above two cases should then be included in this series is, therefore, a matter of opinion. However, as the diagnosis was made by the pathologist, they have been considered as belonging to this group of lip malignancies.

Histological grading was given, along with the type of carcinoma, in nearly all cases. Those that were not so graded were considered as belonging to grade I. Although no rigid criteria were established for the grading, the pathological

work was done for the main part, by either one or other of two histopathologists. The results are given in Table IV.

TABLE IV.  
HISTOLOGICAL GRADING

	Diagnosis	No. of cases	Percentage
Epidermoid Carcinoma	Grade I.	271	50.7
	Grade II.	232	43.4
	Grade III.	26	4.9
Others	Basosquamous carcinoma	1	1.0
	Bowen's disease	1	
	Carcinoma <i>in situ</i>	1	
	Basal cell carcinoma	2	
Totals . . . . .		534	100.0

*Staging.*—There is still no nationally or internationally accepted method of staging. For the purpose of this survey, the method employed at the Holt Radium Institute<sup>5</sup> and other centres in England was adopted. This is as follows.

Stage I. The primary has not spread beyond the tissue of origin to such an extent as to produce definite clinical evidence of loss of mobility or function in the affected part. The area must not measure more than 3 cm. across its greatest dimension. There must be no palpable cervical lymph nodes.

Stage II. The primary has spread beyond the tissue of origin to the above extent, *e.g.*, loss of mobility or function, fixation to the underlying muscle or bones, or radiographic evidence of bone involvement. There must be no palpable cervical lymph nodes.

Stage III. As in 1 or 2, but unilateral lymph nodes of malignant type are present without definite evidence of extra-capsular spread.

Stage IV. (a) As I or II with lymph nodes of malignant type and definite evidence of extra-capsular spread. (b) Bilateral lymph nodes. (c) Remote metastases. (d) Severe cachexia or toxæmia.

By far the greatest number of cases fell into the Stage I group as would be expected—Table V.

TABLE V.  
CLINICAL STAGING

	No. of cases	Per- centage
Stage I. (less than 3 cm. in size) . . .	481	90.1
Stage II. (over 3 cm. in size) . . . . .	35	6.6
Stage III. (with significant nodes) . .	15	2.8
Stage IV. (far advanced disease) . .	3	0.5
Totals . . . . .	534	100

*Metastases.*—Only 18 of the patients (15 patients with Stage III lesions, and 3 patients with Stage IV lesions), or 3.4%, had lymph nodes which were malignant when the patient was first seen. Many others had lymph nodes palpable in the submental or submaxillary areas which were clinically suspicious, but as time elapsed, their innocence became apparent. The criteria for those considered malignant was not as rigid as one would wish. However, if the node continued to enlarge, became fixed, and eventually progressed to kill the patient, they were classified as being malignant, even though no biopsy was obtained. Furthermore, some of the nodes were incised or excised and a pathological examination was made. This procedure was adopted on 6 patients, *i.e.*, those who had either a partial or complete block dissection, local excision, or in one case, a radon gold seed implant. When the above two groups are taken from the original 18 patients, there remain only 2 patients about whom the diagnosis is in doubt. The criteria for these 2 patients were as follows: a hard node in the immediate lymph drainage area which was increasing in size, not painful, and not connected with any other demonstrable cause.

These 18 patients, on the average, had delayed seeking medical attention for 23 months as compared to 4.8 months for the patient without lymph node involvement. One patient, however, had delayed only 2 months, while several had waited for 3 years. As would be expected, very few of these had a histological grade I cancer. In fact, there were only 4 belonging to that grade. The majority, 12 cases, were grade II, while the remainder, or 2 patients, had a histological grade III lesion.

After successful treatment of the primary lesion, lymph node metastases may become apparent. The interval between the treatment of the primary and the appearance of the secondary lesion varies considerably. In this series, 16 patients developed malignant lymph nodes, that is, 3%. The interval between the treatment of the lip primary and the development of the secondary deposit in the lymph node varied from 2 months to 45 months. The same criteria for metastatic malignancy were adopted in this as for the previous group. In this case, there were 11 patients who died from cancer, 3 who had either a block dissection or an incisional biopsy, and only 2 who were left in

the indefinite group. A summary of these two groups of patients who had metastatic malignancy is given in Table VI.

TABLE VI.  
LYMPH NODE METASTASES:  
MALIGNANT LYMPH NODES  
PRESENT WHEN ORIGINALLY SEEN

No. of pts.	Average duration of primary	Grade of primary with number of pts.	Method of diagnosis
18	23 months (2-36 months)	Grade I. 4 Grade II. 12 Grade III. 2	Died from Ca. 10 Pathological 6 Clinical 2

MALIGNANT LYMPH NODES  
WHICH SUBSEQUENTLY DEVELOPED

No. of pts.	Grade of primary with No. of pts.	Interval between treat. of primary and develop. of secondary	Method of diagnosis
16	Grade I. 7 Grade II. 7 Grade III. 2	Average 21 mos. (from 2-45 mos.)	Died from Ca. 11 Histologically 3 Clinical 2

*Treatment.*—The treatment was carried out by the members of the respective clinics. Varieties of methods were used, but the majority of patients were treated by either x-radiation or radium implants. Table VII is a summary of the treatment methods.

TABLE VII.  
TREATMENT METHODS

Radium implants . . . . .	349
X-radiation . . . . .	115
Miscellaneous treatment methods:	
Radon gold seed implants and x-radiation . . .	21
Radon gold seed implants . . . . .	14
Electro desiccation and radon gold seed implants . . . . .	13
Surgical excision alone . . . . .	9
Surface plaque . . . . .	4
Radium implant and x-radiation . . . . .	4
Radon plaque and gold seed implant . . . . .	3
Radon vaselin, radium bomb and gold seed implant . . . . .	1
Radium implant, gold seed implant and x-radiation . . . . .	1
—	70
Total . . . . .	534

There were not enough patients treated by any one of the miscellaneous treatment methods to form an opinion as to the value of the par-

ticular treatment. With the other two methods, however, we have a moderately large number of patients in each group from which we may draw some conclusions. The particular method chosen depended somewhat on the inclination of the therapist, but it also depended to some extent on the type of case, for example, those who had far advanced disease, or those who had major lesions were treated by x-radiation, as illustrated in Table VIII.

TABLE VIII.  
SELECTION OF CASES  
BETWEEN RADIUM IMPLANT AND X-RADIATION

	X-radiation		Radium implant	
	No. of pts.	% of group	No. of pts.	% of group
Stage I . . . . .	103	89.5	326	93.4
Stage II . . . . .	5	4.3	20	5.9
Stage III . . . . .	5	4.3	2	0.6
Stage IV . . . . .	2	1.7	1	0.3
Totals . . . . .	115	100.0	349	100.0

It is seen that a greater percentage of Stage I and Stage II lesions were treated by means of radium implants, whereas more patients with Stage III and IV lesions were treated by x-radiation. However the bias is not great.

*Recurrences.*—It is often difficult to distinguish a new lesion from a recurrence particularly when it occurs near the edge of a previously treated area. Consequently, in this analysis, all cancerous lesions which subsequently developed on the lips have been termed recurrent disease. Some of these were undoubtedly new lesions since they occurred on the opposite side of the lip or, in one case, on the opposite side of the upper lip whereas the original lesion was on the lower.

There were 28 patients, or 5.2%, who thus developed a "recurrence". They developed their "recurrences" anywhere from 6 months to 10 years after the treatment of the original lesions. It is also felt that some of these very late "recurrences" were undoubtedly new lesions.

In the final analysis, those patients who had developed a "recurrence" after treatment of the primary and who have not yet been followed for a period of 5 years were classed as treatment failures. Treatment of these recurrent lesions was divided equally between surgical excision and further radiotherapy. An

argument has been advanced for surgical excision as the treatment of choice for primary cancer of the lip by Cole.<sup>6</sup> He believes that if surgery is necessary to effect a cure of a recurrence the piece of lip which must be removed to be clear of the previously radiated zone, is usually so great that either a serious defect is left in the lip or some type of plastic reconstruction is necessary. Admittedly this is true in a few cases but only 14 of 534 were subjected to subsequent surgery in this series. To submit the other 520 patients to surgery primarily which has equally as high a recurrence rate, (Cross *et al.*<sup>3</sup>), does not seem justified.

**Results.**—In calculating the net end-results the accepted method of subtracting those cases who died from intercurrent disease without evidence of cancer or those who have been lost to follow-up, has been adopted. The following table illustrates the method by giving the net 5 year end-results in this series of 534 patients.

TABLE IX.\*  
FIVE YEAR END RESULTS IN CANCER OF THE LIP  
SASKATCHEWAN CANCER CLINIC

Total number of patients treated (to end of 1943)...	534
Indeterminate group:	
Died of other causes and without recurrence.	42
Lost track of without recurrence.....	16
Total number of indeterminate group.....	58
Determinate Group (total No. minus indeterminate group).....	476
Failures:	
Dead as a result of cancer.....	29
Well but have had a recurrence within 5 years	21
Total number of failures of original treatment.....	50
Successful results:	
Free from disease after 5 years or more.....	426
FIVE YEAR END RESULTS:	
Successful results divided by determinate group	426
— = 89.5%	
476	
Gross Survival—well 5 years following original treatment 447	
— = 94%	
476	

\*Modified from Martin *et al.*<sup>1</sup>

Such a table by itself, however, does not explain the whole picture. If this table is compared with reports from elsewhere<sup>1, 3, 5, 7</sup> the net end results discussed in this paper appear much better. However, when we look at the end result

by stage of the disease, an explanation for the higher figure is obtained, Table X.

TABLE X.  
FINAL RESULTS BY STAGES

	Number of patients treated	5 year net survival
Stage I.....	479	93%
Stage II.....	36	69%
Stage III.....	15	33%
Stage IV.....	3	0%

For comparison the final results by stages as reported by the Holt Radium Institute, Manchester (1934 to 1938)<sup>5</sup> is given. These results have been chosen for comparison since the same method of staging has been employed in each group.

TABLE XI.  
FINAL RESULTS BY STAGES  
HOLT RADIUM INSTITUTE, MANCHESTER  
1934 - 1938

	Number of patients treated	5 year net survival
Stage I.....	89	79%
Stage II.....	58	67%
Stage III.....	17	27%
Stage IV.....	11	11%

Whenever ionizing radiation is used for the treatment of a particular disease, preference is usually given by the therapist to a particular means of administering that radiation. Some therapists prefer radium, either as moulds or as interstitial implants, while others prefer the use of x-radiation.<sup>8, 9</sup> Table XII is a technique analysis between the two most frequently used methods in this series.

TABLE XII.  
TECHNIQUE ANALYSIS

Technique	Number of patients treated	5 year net survival
X-radiation.....	115	85%
Radium implant.....	349	91%

The 6% difference shown between the two techniques may be statistically insignificant. As pointed out before there was a bias toward using radium implantation for Stage I and Stage II lesions. Furthermore, the number of patients placed in the indeterminate group as having died from intercurrent disease was proportionately much greater in the x-radiation

group—20 patients out of 115—whereas there were only 16 out of 349 in the radium implant group. This would seem to indicate a further degree of selection, *i.e.*, older patients, or those whose general condition was poor, were treated by means of x-radiation.

**Cosmetic results.**—No discussion regarding the treatment of cancer of the lip would be complete without mention of the final cosmetic result. One of the most serious criticisms to the surgical treatment of cancer of the lip is the resulting scar and occasional puckering of the lip which occurs. In general, the cosmetic result following properly administered radiation is good. Certain factors, however, have been observed to lead to defects in the treated area. For instance, improper removal of tissue for pathological examination by using transverse instead of vertical incisions will cause such a defect. The development of a secondary infection during the radiation reaction tends to cause an excess of tissue damage. Finally the improper placing of radium needles during an implant may cause an intense zone of irradiation leading to a localized necrosis which heals only slowly leaving a depressed scar.

TABLE XIII.  
DIED AS A RESULT OF CANCER

Died of cervical lymph node metastases which were present when the patient was originally seen	
Stage III.....	10
Stage IV.....	3
	13
Died from cervical metastases which subsequently developed.....	12
Died postoperatively following a block dissection of cervical nodes.....	1
Died from visceral metastases (as stated on death certificate although there was no post mortem examination).....	2
Details not known—cause of death as stated on death certificate "Cancer of lip".....	1
Total.....	29

## CONCLUSIONS

1. Cancer of the lip can be cured by radiotherapy in a very high percentage of cases provided treatment is instituted early.

2. The choice of a particular radiotherapeutic technique is not important provided meticulous care in the planning and execution of that technique is taken. This is necessary to minimize the recurrence rate and to insure good cosmetic results.

3. Radiotherapy is not the treatment of choice for metastatically involved lymph nodes. In the present series, three patients were said to have been "cured" by radiotherapy but only one of these had histologically proved cancer in the nodes. Greater success is obtained by a radical block dissection. Douglas<sup>10</sup> quotes a figure of 44% net five year survivals in this respect.

4. Prophylactic block dissections are not indicated. Figi,<sup>11</sup> while doing 549 prophylactic operations, found metastatic nodes in only 91 (16.5%). In this series only 34 patients (6.3%) had secondarily involved nodes at any time (15 patients in stage III; 3 patients in stage IV; and 16 patients who subsequently developed nodes). Even the operative mortality of 5% is nearly as great as the risk of developing nodes. When one is able to receive patients with early disease, then an intelligent follow-up system proved satisfactory.

## SUMMARY

The result of treating 534 consecutive cases by radiotherapy is reviewed: The overall 5 year net survival was 89.5%. From a study of these cases, cancer of the lip is discussed from the standpoint of etiology, pathology, metastases, and the choice of radiotherapeutic technique.

## REFERENCES

- MARTIN, H., MACCOMB, W. S. AND BLADY, J. V.: *Ann. Surg.*, 114: 226, 1941.
- ACKERMAN, L. V. AND DEL REGATO, J. A.: *Cancer, Diagnosis, Treatment and Prognosis*, C. V. Mosby Co., 1947.
- CROSS, J. E., GURALNICK, E. AND DALARD, E. M.: *Surg., Gynec. & Obst.*, 87: 153, 1948.
- HOWES, W. E. AND LAROSA, F. J.: *Am. J. Roentgenol.*, 47: 37, 1942.
- Idem*: *Am. J. Roentgenol.*, 60: 763, 1948.
- The Results of Radium and X-ray Therapy in Malignant Disease, Second Statistical Report from the Holt Radium Institute, Manchester, E. & S. Livingstone, Ltd., 1946.
- COLE, P. C.: *Brit. J. Surg.*, 36: 79, 1948.
- RICHARDS, G. E.: *Canad. M. A. J.*, 35: 490, 1936.
- PATERSON, R.: *The Treatment of Malignant Disease by Radium and X-rays*, Edward Arnold & Co., London, 1948.
- SMITHERS, D. W.: *Post-Grad. M. J.*, November, 1939.
- DOUGLAS, W. D.: Personal communication.
- FIGI, F. A.: *Surg., Gynec. & Obst.*, 59: 810, 1934.

Experimental Aortic Anastomosis, Glenn, F. and others, *Proc. Soc. Exper. Biol. & Med.*, 71: 619, 1949. Seven young dogs between the ages of three and eight weeks were subjected to end-to-end anastomosis of the thoracic aorta. Three of these dogs survived and were studied approximately one year after operation to determine the status of the site of anastomosis. Narrowing of the aortic lumen at the suture line was demonstrated in each animal by angiocardiographic methods and also in one animal at thoracotomy. This is of significance in that with the resection and anastomosis operation for coarctation of the aorta, an aortic lumen may be established at the anastomosis which is satisfactory for a child of a few years of age, but would probably be insufficient in size when the patient grows to maturity.